

**REMARKS**

Claims 1-10, 20-23, and 27-33 are pending in the instant application. Claims 1-4 and 7 have been rejected. Claims 1, 2 and 7 have been objected to. Claims 1 and 2 have been cancelled. Claims 3 and 7 have been amended. These amendments do not introduce any new matter, and support for them can be found in the specification. Claims 8-10, 20-23, and 27-33 have been cancelled as they are drawn to non-elected subject matter. After entry of this amendment, Claims 3-7 will be pending.

**Objection to Claims 1, 2 and 7**

The Examiner has rejected Claims 1, 2 and 7 for containing non-elected subject matter. Applicants respectfully traverse the Examiner's objection. In Applicant's response, dated March 26, 2007, the Applicants elected Group I, which contains Claims 1-7. According, Applicants respectfully request that the objection of Claims 1, 2 and 7 be withdrawn.

**Rejection of Claims 1-4 and 7 under 35 USC §112, first paragraph**

**Written Description**

The Examiner has rejected Claims 1-4 and 7 under 35 U.S.C §112, first paragraph for allegedly failing to comply with the written description requirement. Specifically the Examiner stated that:

The specification does not describe with sufficient detail to allow a person skilled in the art to conclude the applicant was in possession of the claimed invention. In order to adequately describe a broad generic claim, a sufficient number of representative species that reflect the variation within that genus must be disclosed (MPEP 2163). An adequate description of the representative species may be obtain through (a) actual reduction to practice, (b) reduction to drawings or structural chemical formulas; (c) disclosure of relevant, identifying characteristics by functional characteristics coupled with known or disclosed correlations between function and structure (MPEP 2163.02).

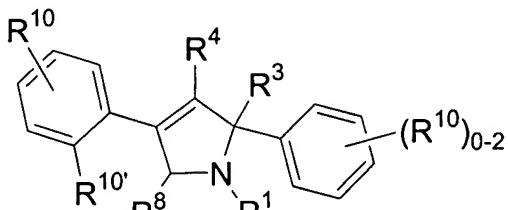
In the instant case, Applicants are claiming a large genus of compounds with substantial structural variations in Claims 1-4. The disclosure is limited to a

limited number of compounds reduced to practice, which is not an adequate representation of the genus. Below is an analysis, which compares the scope of the claim and the scope of the description to determine whether Applicants demonstrated possession of the invention:

**Scope of the Claims:**

Claims 1-3, 7: Compounds of Formula III (see structure below), salt stereoisomer, or pharmaceutical composition thereof;  $R^1$ ,  $R^3$ ,  $R^4$ ,  $R^8$ ,  $R^{10}$ , and  $R^{10'}$  as defined in Claim 3.

Claim 4: Compounds of Formula III (see structure below), salt stereoisomer, or pharmaceutical composition thereof;  $R^1$ ,  $R^3$ ,  $R^4$ ,  $R^8$ ,  $R^{10}$ , and  $R^{10'}$  as defined in Claim 3.



III

**Scope of the Disclosure:**

Reduction to Practice: a *limited* set of compounds *representing* the following substitutions,

$R^1$  = (C=O)O-C1-C10 alkyl, (optionally substituted with amino, dimethylamino or alkyl)

(C=O)O-phenyl, (unsubstituted)

(C=O)O-pyrrolidine or (C=O)O-piperidine (both unsubstituted)

$R^{3,4,8}$  = H, Me

$R^{10}$  = halogen

$R^{10'}$  = halogen

Without conceding the correctness of the Examiner's argument, but to advance the prosecution of the instant application, applicants have cancelled Claims 1 and 2. In light of these cancellations, the rejection of Claims 1 and 2 should be rendered moot.

However, Applicants respectfully traverse rejection of Claims 3, 4 and 7.

For a written description rejection, the Examiner has the "initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure of the invention defined by the claims." MPEP 2163.04 (citing *In re Wertheim*, 191 USPQ 90, 97(1976)). For Claims 3, 4 and 7, the Examiner has not met this initial burden of establishing a reasonable basis for questioning the Applicants completion of the written description requirement.

In the instant case, the Examiner contends that Applicants actually reduced to practice a limited number compounds in Claims 1-4 and 7, which was not a sufficient representation of the large number of compounds encompassed by the claims. In particular, the Examiner asserted that the substituents  $R^1$ ,  $R^3$ ,  $R^4$ ,  $R^8$ ,  $R^{10}$ , and  $R^{10'}$  were not adequately represented by the specification. Applicants respectfully contend that the examples provided in the specification adequately describe all of the aforementioned substituents in the claims. The Examiner stated that the Applicants merely reduced to practice one example of a  $R^{10}$  substitution, namely a halogen. However, Applicants respectfully maintain that the examples section of the specifications illustrates at least six embodiments of  $R^{10}$  substitutions.

Representative examples are illustrated below:

1.  $(C=O)_aObC1-C10$  alkyl: Exemplified by Compounds 1-8 and 1-10 (pg. 63) - Ethyl and isopropyl, respectively, substituted on  $R^1$
2.  $(C=O)_aObaryl$ : Exemplified by Compound 1-9 (pg. 63) - Phenyl substituted on  $R^1$
3.  $C2-C10$  alkenyl: Exemplified by Compound 1-7 (pg. 63) – Allyl substituted on  $R^1$
4.  $(C=O)_aOb$  heterocyclyl: Exemplified by Compounds 2-10 and 2-11 (pg. 69-70) - Pyrrolidinyl and piperidinyl, respectively, substituted on  $R^1$
5. Halogen: Compounds 1-7 thru 1-10 and 2-8 thru 2-11 (pg. 63, 69-70) - F substituted on Phenyl Group

6. O<sub>a</sub>(C=O)bNR<sup>12</sup>R<sup>13</sup>: Exemplified by Compounds 2-8 and 2-9 (pg. 69) –  
Amino groups substituted on R<sup>1</sup>

The Applicants also maintain that adequate support exists in the specifications for all of the substituents including, but not limited to R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>8</sup>, and R<sup>10</sup>. For example, Claim 3 provides four possible substituents for R<sup>1</sup>, three of which are described in the specification either as a compound that has been actually reduced to practice (pg. 64) or listed as a preferred substitution (pg. 20). Similarly, Claim 3 provides three possible substituents for R<sup>3</sup>, R<sup>4</sup>, R<sup>8</sup>, two of which were listed as preferred selections in the specification (pg. 20). Finally, Claim 3 narrowly defines R<sup>10</sup> as halogen and the specification lists fluoro as a preferred substituent (pg. 21).

According to the MPEP, the written description requirement for a claimed genus may be satisfied through a sufficient description of a representative number of species (2163.05). If the genus contains substantial variation, the Applicant must "describe a sufficient variety of species to reflect the variation within the genus" (MPEP 2163.05). Although the MPEP does not specify what constitutes a "representative number of species", typically more than one embodiment is required to satisfy the written description requirement. In the instant application, Applicants have provided a significantly more than the requisite number of embodiments to ensure that the variation within the species is reflected.

Applicants maintain that the Examiner has not made a *prima facie* case of lack of written description, and in light of the arguments presented, it is not reasonable to conclude that Applicants have not sufficiently described the claims. Accordingly, Applicants respectfully request the rejection of Claims 3, 4, and 7 under 35 U.S.C. §112, first paragraph, be withdrawn.

Enablement

The Examiner has also rejected claims 1-4 and 7 under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in a manner to enable one skilled in the art to make and/or use the invention. Specifically the Examiner stated that:

The specification does not contain sufficient disclosure to one skilled in the art to "practice the invention commensurate in scope with the breath of the claims."

The specification does not meet the enablement requirement when undue experimentation is required to practice the invention. *Mineral Separation v.*

*Hyde*, 242 U.S. 261, 270 (1916). The MPEP states that several factors such be considered to determine if the disclosure satisfies the enablement requirement and whether experimentation is undue. The factors to be considered are the (1) breadth of the claim, (2) nature of invention, (3) state of prior art, (4) level of ordinary skill, (5) level of predictability, (6) amount of direction provided by the inventor, (7) existence of working examples, and (8) quantity of experimentation needed to make or use the invention (MPEP 2164.01(a)).

In the instant application, the Examiner states that due to the low level of predictability in the art, absent guidance, one of ordinary skill would not expect that all of the compounds encompassed by the genus would have activity. Since one of ordinary skill would not know which compounds not exemplified would possess the claimed activity, a skilled artisan would be subject to undue experimentation to determine which compounds in the broad genus claimed would have activity required to practice the invention.

Without conceding the correctness of the Examiner's argument, but to advance the prosecution of the instant application, applicants have cancelled Claims 1 and 2. In light of these cancellations, the rejection of Claims 1 and 2 should be rendered moot.

However, Applicants respectfully traverse the rejection of Claims 3, 4 and 7.

In order to make a rejection based upon lack of enablement, the Examiner has the initial burden to explain why the scope of protection provided by a claim is not adequately enabled by the disclosure (MPEP 2164.04). The specification disclosure which contains a teaching of the manner and process of making and using the invention...must be taken as being in compliance with the enablement requirement...unless there is a reason to doubt the objective truth of the statement (MPEP 2164.04). In the instant application, the Examiner states that due to the low level of predictability in the art, a person skilled in the art would be subjected to undue experimentation to determine which compound would possess activity. The applicant disagrees with the Examiner's allegation.

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (MPEP 2164.01). "An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or

guidance." *In re Colianni*, 195 USPQ 150, 153 (1977). "[A] considerable amount of experimentation is permissible...if the specification in question provides a reasonable amount to guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 8 USPQ2d 1400, 1404 (1988). In the instant case, Applicants have provided five generic schemes that can be used for guidance in making compounds of the present invention (pg. 24-28) and included detailed instructions of how to synthesize ten compounds that were reduced to practice (pg. 61-70). According to the MPEP, as long as the specification discloses *at least one* method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied (MPEP 2164.01(b), emphasis added). These examples clearly provide guidance to one skilled in the art how to proceed with further experimentation. One skilled in the art, after reading the disclosure would not have to engage in undue experimentation

Applicants maintain that the Examiner has not made a *prima facie* case of nonenablement, and in light of the argument presented, it is not reasonable to conclude that the Applicant has not enabled the claims. Accordingly, Applicants respectfully request the rejection of Claims 3, 4, and 7 under 35 U.S.C. §112, first paragraph, be withdrawn.

Rejection of Claims 1-4 and 7 under 35 USC §112, second paragraph

The Examiner rejected Claims 1-4 and 7 under 35 U.S.C. 112, second paragraph for being indefinite and failing to point out and distinctly claim the subject matter the applicant regards as the invention. Specifically, the Examiner indicated that the 14<sup>th</sup> and 16<sup>th</sup> option for R<sup>10</sup> in the claims would violate with the valence requirement. Without conceding the correctness of the Examiner's argument, but to advance the prosecution of the instant application, Applicants have amended Claim 1-4 and 7 to remove Option 14 and 16 under R<sup>10</sup>. In light of these amendments, this rejection should be rendered moot. Accordingly, Applicants respectfully request the rejection of claims 1-4 and 7 under 35 U.S.C. §112, second paragraph, be withdrawn.

If a telephonic communication with the Applicants' representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

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